Title: Sensorimotor and cortical-cerebellar lateralization in autism spectrum disorder

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Introduction: Sensorimotor abilities are disrupted in the majority of individuals with autism spectrum disorder (ASD; Fournier et al., 2010) and are strongly related to functional outcomes (Travers et al., 2017). Atypical lateralization of sensorimotor functioning, including increased rates of mixed-handedness (Escalante-Mead et al., 2003) and reduced lateralized dominance of upper limb movements (Paquet et al., 2016), has been documented implicating reduced hemispheric specialization of cortical-cerebellar networks supporting sensorimotor action. While sensorimotor behavioral studies suggest characterization of brain network lateralization in ASD may provide new information on neurodevelopmental processes associated with the disorder, lateralization of sensorimotor brain networks during behavior has not been systematically assessed in patients. In the present study, we examined sensorimotor behavior and brain activation during left- and right-handed gripping in individuals with ASD to assess lateralization of sensorimotor behavior and brain function.

Method: Forty-one individuals with ASD, including 8 left-handed individuals, and twenty-eight typically developing (TD) controls, including 3 left-handed individuals, matched on age (range: 10-34 years) and sex completed a visually guided precision gripping task during fMRI. During the task, participants gripped a force transducer while viewing two horizontal bars. Their task was to press on the transducer to move the lower "force" bar upwards to the height of the static "target" bar. The target bar was set at 45% of each individual's maximum voluntary contraction (MVC). Participants completed three 26-s blocks of gripping each separated by 26-s of rest. They completed one run of the task with each hand. Mean force, force complexity (approximate entropy, or ApEn), and force variability were examined separately for each hand. Percent BOLD signal change during gripping vs. rest was examined ($p < .005$; $\alpha < .05$; $k > 50$ voxels). To determine the relation of manual and brain network lateralization with functional motor abilities, participants completed the Bruininks-Oseretsky Test of Motor Proficiency, Second Edition (BOT-2). To assess relationships of sensorimotor performance and functional abilities, the Vineland Adaptive Behavior Scales, Third Edition (VABS) also was administered.

Results: Individuals with ASD showed greater force variability compared to controls, though these motor differences between groups varied as a function of hand. Individuals with ASD showed increased force variability during dominant hand gripping relative to TD controls ($p = .033$), while the two groups showed similar levels of non-dominant hand force variability. During fMRI testing, both individuals with ASD and TD controls showed increased brain activation in left primary (striate) and secondary (extrastriate) visual cortices, but striate and extrastriate activation differed across right and left hands, and these lateralized differences were stronger in TD controls. Specifically, in TD controls, activation in both left striate and extrastriate was increased during left- compared to right-hand gripping, whereas striate and extrastriate activation was similar for left- and right-hand gripping for individuals with ASD. In TD controls only, increased activation in left striate during right hand gripping was associated with reduced force variability and increased force complexity as well as greater fine motor precision on the BOT-2. On the BOT-2, relative to TD controls, individuals with ASD showed reduced fine motor precision, manual dexterity, bilateral coordination, balance, and body coordination. For individuals with ASD, increased force variability was associated with reduced VABS-rated functional abilities.

Discussion: Our finding of increased dominant hand variability in ASD suggests reduced lateralization of precision fine motor control. This is consistent with prior studies demonstrating atypical development of handedness and upper limb movement in ASD and indicates that lateralization of sensorimotor function may be an important quantitative trait of ASD. Our fMRI results identified atypical lateralization of visual cortical circuits during precision manual motor behavior in ASD. Specifically, we found that individuals with ASD fail to show lateralized increases of left striate and extrastriate activation during left hand gripping as seen in controls suggesting deficient hemispheric specialization of visual procession circuits that may impair the development of lateralized motor abilities. Our finding that increased force variability in ASD is associated with reduced adaptive function further

indicates that sensorimotor issues may impact a range of daily living skills in ASD and may be more central to the disorder than previously believed.

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